

OIEP

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/676,436

DATE: 11/07/2001

TIME: 15:14:33

Input Set : A:\RTS-0169\_Seq\_ASCII.txt

Output Set: N:\CRF3\11072001\I676436.raw

3 <110> APPLICANT: Donna T. Ward  
 4 William Gaarde  
 5 Brett P. Monia  
 6 Jacqueline Wyatt  
 8 <120> TITLE OF INVENTION: ANTISENSE MODULATION OF MEKK4 EXPRESSION  
 10 <130> FILE REFERENCE: RTS-0169  
 C--> 12 <140> CURRENT APPLICATION NUMBER: US/09/676,436  
 C--> 12 <141> CURRENT FILING DATE: 2000-09-29  
 12 <160> NUMBER OF SEQ ID NOS: 89  
 15 <210> SEQ ID NO: 1  
 16 <211> LENGTH: 20  
 17 <212> TYPE: DNA  
 18 <213> ORGANISM: Artificial Sequence ✓  
 W--> 20 <220> FEATURE:  
 20 <223> OTHER INFORMATION: Antisense Oligonucleotide ✓  
 22 <400> SEQUENCE: 1  
 23 tccgtcatcg ctcctcaggg  
 26 <210> SEQ ID NO: 2  
 27 <211> LENGTH: 20  
 28 <212> TYPE: DNA  
 29 <213> ORGANISM: Artificial Sequence ✓  
 W--> 31 <220> FEATURE:  
 31 <223> OTHER INFORMATION: Antisense Oligonucleotide ✓  
 33 <400> SEQUENCE: 2  
 34 atgcattctg cccccaagga  
 37 <210> SEQ ID NO: 3  
 38 <211> LENGTH: 4990  
 39 <212> TYPE: DNA  
 40 <213> ORGANISM: Homo sapiens  
 42 <220> FEATURE:  
 43 <221> NAME/KEY: CDS  
 44 <222> LOCATION: (1)...(4476)  
 46 <400> SEQUENCE: 3  
 47 cta gaa gac ttc tcc gat gaa aca aat aca gag aat ctt tat ggt acc 48  
 48 Leu Glu Asp Phe Ser Asp Glu Thr Asn Thr Glu Asn Leu Tyr Gly Thr  
 49 1 5 10 15  
 51 tct ccc ccc agc aca cct cga cag atg aaa cgc atg tca acc aaa cat 96  
 52 Ser Pro Pro Ser Thr Pro Arg Gln Met Lys Arg Met Ser Thr Lys His  
 53 20 25 30  
 55 cag agg aat aat gtg ggg agg cca gcc agt cgg tct aat ttg aaa gaa 144  
 56 Gln Arg Asn Asn Val Gly Arg Pro Ala Ser Arg Ser Asn Leu Lys Glu  
 57 35 40 45  
 59 aaa atg aat gca cca aat cag cct cca cat aaa gac act gga aaa aca 192  
 60 Lys Met Asn Ala Pro Asn Gln Pro Pro His Lys Asp Thr Gly Lys Thr  
 61 50 55 60  
 63 gtg gag aat gtg gaa gaa tac agc tat aag cag gag aaa aag atc cga 240  
 64 Val Glu Asn Val Glu Glu Tyr Ser Tyr Lys Gln Glu Lys Lys Ile Arg

ENTERED

20  
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20

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65	65	70	75	80	
67	gca gct ctt aga aca aca gag cgt gat cat aaa aaa aat gta cag tgc				288
68	Ala Ala Leu Arg Thr Thr Glu Arg Asp His Lys Lys Asn Val Gln Cys				
69		85	90	95	
71	tca ttc atg tta gac tca gtg ggt gga tct ttg cca aaa aaa tca att				336
72	Ser Phe Met Leu Asp Ser Val Gly Gly Ser Leu Pro Lys Lys Ser Ile				
73		100	105	110	
75	cca gat gtg gat ctc aat aag cct tac ctc agc ctt ggc tgt agc aat				384
76	Pro Asp Val Asp Leu Asn Lys Pro Tyr Leu Ser Leu Gly Cys Ser Asn				
77		115	120	125	
79	gct aag ctt cca gta tct gtg ccc atg cct ata gcc aga cct gca cgc				432
80	Ala Lys Leu Pro Val Ser Val Pro Met Pro Ile Ala Arg Pro Ala Arg				
81		130	135	140	
83	cag act tct agg act gac tgt cca gca gat cgt tta aag ttt ttt gaa				480
84	Gln Thr Ser Arg Thr Asp Cys Pro Ala Asp Arg Leu Lys Phe Phe Glu				
85	145	150	155	160	
87	act tta cga ctt ttg cta aag ctt acc tca gtc tca aag aaa aaa gac				528
88	Thr Leu Arg Leu Leu Leu Lys Leu Thr Ser Val Ser Lys Lys Lys Asp				
89		165	170	175	
91	agg gag caa aga gga caa gaa aat acg tct ggt ttc tgg ctt aac cga				576
92	Arg Glu Gln Arg Gly Gln Glu Asn Thr Ser Gly Phe Trp Leu Asn Arg				
93		180	185	190	
95	tct aac gaa ctg atc tgg tta gag cta caa gcc tgg cat gca gga cgg				624
96	Ser Asn Glu Leu Ile Trp Leu Glu Leu Gln Ala Trp His Ala Gly Arg				
97		195	200	205	
99	aca att aac gac cag gac ttc ttt tta tat aca gcc cgt caa gcc atc				672
100	Thr Ile Asn Asp Gln Asp Phe Phe Leu Tyr Thr Ala Arg Gln Ala Ile				
101		210	215	220	
103	cca gat att att aat gaa atc ctt act ttc aaa gtc gac tat ggg agc				720
104	Pro Asp Ile Ile Asn Glu Ile Leu Thr Phe Lys Val Asp Tyr Gly Ser				
105	225	230	235	240	
107	ttc gcc ttt gtt aga gat aga gct ggt ttt aat ggt act tca gta gaa				768
108	Phe Ala Phe Val Arg Asp Arg Ala Gly Phe Asn Gly Thr Ser Val Glu				
109		245	250	255	
111	ggg cag tgc aaa gcc act cct gga aca aag att gta ggt tac tca aca				816
112	Gly Gln Cys Lys Ala Thr Pro Gly Thr Lys Ile Val Gly Tyr Ser Thr				
113		260	265	270	
115	cat cat gag cat ctc caa cgc cag agg gtc tca ttt gag cag gta aaa				864
116	His His Glu His Leu Gln Arg Gln Arg Val Ser Phe Glu Gln Val Lys				
117		275	280	285	
119	cgg ata atg gag ctg cta gag tac ata gaa gca ctt tat cca tca ttg				912
120	Arg Ile Met Glu Leu Leu Glu Tyr Ile Glu Ala Leu Tyr Pro Ser Leu				
121		290	295	300	
123	cag gct ctt cag aag gac tat gaa aaa tat gct gca aaa gac ttc cag				960
124	Gln Ala Leu Gln Lys Asp Tyr Glu Lys Tyr Ala Ala Lys Asp Phe Gln				
125	305	310	315	320	
127	gac agg gtg cag gca ctc tgt ttg tgg tta aac atc aca aaa gac tta				1008
128	Asp Arg Val Gln Ala Leu Cys Leu Trp Leu Asn Ile Thr Lys Asp Leu				
129		325	330	335	

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131	aat	cag	aaa	tta	agg	att	atg	ggc	act	gtt	ttg	ggc	atc	aag	aat	tta	1056
132	Asn	Gln	Lys	Leu	Arg	Ile	Met	Gly	Thr	Val	Leu	Gly	Ile	Lys	Asn	Leu	
133				340				345						350			
135	tca	gac	att	ggc	tgg	cca	gtg	ttt	gaa	atc	cct	tcc	cct	cga	cca	tcc	1104
136	Ser	Asp	Ile	Gly	Trp	Pro	Val	Phe	Glu	Ile	Pro	Ser	Pro	Arg	Pro	Ser	
137				355				360						365			
139	aaa	ggt	aat	gag	ccg	gag	tat	gag	ggt	gat	gac	aca	gaa	gga	gaa	tta	1152
140	Lys	Gly	Asn	Glu	Pro	Glu	Tyr	Glu	Gly	Asp	Asp	Thr	Glu	Gly	Glu	Leu	
141				370				375						380			
143	aag	gag	ttg	gaa	agt	agt	acg	gat	gag	agt	gaa	gaa	gaa	caa	atc	tct	1200
144	Lys	Glu	Leu	Glu	Ser	Ser	Thr	Asp	Glu	Ser	Glu	Glu	Glu	Gln	Ile	Ser	
145	385						390				395					400	
147	gat	cct	agg	gta	ccg	gaa	atc	aga	cag	ccc	ata	gat	aac	agc	ttc	gac	1248
148	Asp	Pro	Arg	Val	Pro	Glu	Ile	Arg	Gln	Pro	Ile	Asp	Asn	Ser	Phe	Asp	
149					405					410					415		
151	atc	cag	tcg	cgg	gac	tgc	ata	tcc	aag	aag	ctt	gag	agg	ctc	gaa	tct	1296
152	Ile	Gln	Ser	Arg	Asp	Cys	Ile	Ser	Lys	Lys	Leu	Glu	Arg	Leu	Glu	Ser	
153				420					425					430			
155	gag	gat	gat	tct	ctt	ggc	tgg	gga	gca	cca	gac	tgg	agc	aca	gaa	gca	1344
156	Glu	Asp	Asp	Ser	Leu	Gly	Trp	Gly	Ala	Pro	Asp	Trp	Ser	Thr	Glu	Ala	
157				435				440						445			
159	ggc	ttt	agt	aga	cat	tgt	ctg	act	tct	att	tat	aga	cca	ttt	gta	gac	1392
160	Gly	Phe	Ser	Arg	His	Cys	Leu	Thr	Ser	Ile	Tyr	Arg	Pro	Phe	Val	Asp	
161				450				455						460			
163	aaa	gca	ctg	aag	cag	atg	ggg	tta	aga	aag	tta	att	tta	aga	ctt	cac	1440
164	Lys	Ala	Leu	Lys	Gln	Met	Gly	Leu	Arg	Lys	Leu	Ile	Leu	Arg	Leu	His	
165	465					470					475					480	
167	aag	cta	atg	gat	ggt	tcc	ttg	caa	agg	gca	cgt	ata	gca	ttg	gta	aag	1488
168	Lys	Leu	Met	Asp	Gly	Ser	Leu	Gln	Arg	Ala	Arg	Ile	Ala	Leu	Val	Lys	
169					485					490					495		
171	aac	gat	cgt	cca	gtg	gag	ttt	tct	gaa	ttt	cca	gat	ccc	atg	tgg	ggt	1536
172	Asn	Asp	Arg	Pro	Val	Glu	Phe	Ser	Glu	Phe	Pro	Asp	Pro	Met	Trp	Gly	
173				500					505					510			
175	tca	gat	tat	gtg	cag	ttg	tca	agg	aca	cca	cct	tca	tct	gag	gag	aaa	1584
176	Ser	Asp	Tyr	Val	Gln	Leu	Ser	Arg	Thr	Pro	Pro	Ser	Ser	Glu	Glu	Lys	
177				515				520						525			
179	tgc	agt	gct	gtg	tcg	tgg	gag	gag	ctg	aag	gcc	atg	gat	tta	cct	tca	1632
180	Cys	Ser	Ala	Val	Ser	Trp	Glu	Glu	Leu	Lys	Ala	Met	Asp	Leu	Pro	Ser	
181				530				535						540			
183	ttc	gaa	cct	gcc	ttc	cta	gtt	ctc	tgc	cga	gtc	ctt	ctg	aat	gtc	ata	1680
184	Phe	Glu	Pro	Ala	Phe	Leu	Val	Leu	Cys	Arg	Val	Leu	Leu	Asn	Val	Ile	
185	545					550					555					560	
187	cat	gag	tgt	ctg	aag	tta	aga	ttg	gag	cag	aga	cct	gct	gga	gaa	cca	1728
188	His	Glu	Cys	Leu	Lys	Leu	Arg	Leu	Glu	Gln	Arg	Pro	Ala	Gly	Glu	Pro	
189					565					570					575		
191	tct	ctc	ttg	agt	att	aag	cag	ctg	gtg	aga	gag	tgt	aag	gag	gtc	ctg	1776
192	Ser	Leu	Leu	Ser	Ile	Lys	Gln	Leu	Val	Arg	Glu	Cys	Lys	Glu	Val	Leu	
193				580					585					590			
195	aag	ggc	ggc	ctg	ctg	atg	aag	cag	tac	tac	cag	ttc	atg	ctg	cag	gag	1824

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196	Lys	Gly	Gly	Leu	Leu	Met	Lys	Gln	Tyr	Tyr	Gln	Phe	Met	Leu	Gln	Glu	
197			595					600					605				
199	gtt	ctg	gag	gac	ttg	gag	aag	ccc	gac	tgc	aac	att	gac	gct	ttt	gaa	1872
200	Val	Leu	Glu	Asp	Leu	Glu	Lys	Pro	Asp	Cys	Asn	Ile	Asp	Ala	Phe	Glu	
201		610					615				620						
203	gag	gat	cta	cat	aaa	atg	ctt	atg	gtg	tat	ttt	gat	tac	atg	aga	agc	1920
204	Glu	Asp	Leu	His	Lys	Met	Leu	Met	Val	Tyr	Phe	Asp	Tyr	Met	Arg	Ser	
205	625					630					635					640	
207	tgg	atc	caa	atg	cta	cag	caa	tta	cct	caa	gca	tcg	cat	agt	tta	aaa	1968
208	Trp	Ile	Gln	Met	Leu	Gln	Gln	Leu	Pro	Gln	Ala	Ser	His	Ser	Leu	Lys	
209					645					650					655		
211	aat	ctg	tta	gaa	gaa	gaa	tgg	aat	ttc	acc	aaa	gaa	ata	act	cat	tac	2016
212	Asn	Leu	Leu	Glu	Glu	Glu	Trp	Asn	Phe	Thr	Lys	Glu	Ile	Thr	His	Tyr	
213				660					665						670		
215	ata	cgg	gga	gga	gaa	gca	cag	gcc	ggg	aag	ctt	ttc	tgt	gac	att	gca	2064
216	Ile	Arg	Gly	Gly	Glu	Ala	Gln	Ala	Gly	Lys	Leu	Phe	Cys	Asp	Ile	Ala	
217			675					680					685				
219	gga	atg	ctg	ctg	aaa	tct	aca	gga	agt	ttt	tta	gaa	ttt	ggc	tta	cag	2112
220	Gly	Met	Leu	Leu	Lys	Ser	Thr	Gly	Ser	Phe	Leu	Glu	Phe	Gly	Leu	Gln	
221		690					695					700					
223	gag	agc	tgt	gct	gaa	ttt	tgg	act	agt	gcg	gat	gac	agc	agt	gct	tcc	2160
224	Glu	Ser	Cys	Ala	Glu	Phe	Trp	Thr	Ser	Ala	Asp	Asp	Ser	Ser	Ala	Ser	
225	705					710					715					720	
227	gac	gaa	atc	agg	agg	tct	ggt	ata	gag	atc	agt	cga	gcc	ctg	aag	gag	2208
228	Asp	Glu	Ile	Arg	Arg	Ser	Val	Ile	Glu	Ile	Ser	Arg	Ala	Leu	Lys	Glu	
229					725					730					735		
231	ctc	ttc	cat	gaa	gcc	aga	gaa	agg	gct	tcc	aaa	gca	ctt	gga	ttt	gct	2256
232	Leu	Phe	His	Glu	Ala	Arg	Glu	Arg	Ala	Ser	Lys	Ala	Leu	Gly	Phe	Ala	
233				740					745					750			
235	aaa	atg	ttg	aga	aag	gac	ctg	gaa	ata	gca	gca	gaa	ttc	agg	ctt	tca	2304
236	Lys	Met	Leu	Arg	Lys	Asp	Leu	Glu	Ile	Ala	Ala	Glu	Phe	Arg	Leu	Ser	
237			755					760					765				
239	gcc	cca	gtt	aga	gac	ctc	ctg	gat	gtt	ctg	aaa	tca	aaa	cag	tat	gtc	2352
240	Ala	Pro	Val	Arg	Asp	Leu	Leu	Asp	Val	Leu	Lys	Ser	Lys	Gln	Tyr	Val	
241		770					775					780					
243	aag	gtg	caa	att	cct	ggg	tta	gaa	aac	ttg	caa	atg	ttt	gtt	cca	gac	2400
244	Lys	Val	Gln	Ile	Pro	Gly	Leu	Glu	Asn	Leu	Gln	Met	Phe	Val	Pro	Asp	
245	785					790					795					800	
247	act	ctt	gct	gag	gag	aag	agt	att	att	ttg	cag	tta	ctc	aat	gca	gct	2448
248	Thr	Leu	Ala	Glu	Glu	Lys	Ser	Ile	Ile	Leu	Gln	Leu	Leu	Asn	Ala	Ala	
249					805					810					815		
251	gca	gga	aag	gac	tgt	tca	aaa	gat	tca	gat	gac	gta	ctc	atc	gat	gcc	2496
252	Ala	Gly	Lys	Asp	Cys	Ser	Lys	Asp	Ser	Asp	Asp	Val	Leu	Ile	Asp	Ala	
253				820					825					830			
255	tat	ctg	ctt	ctg	acc	aag	cac	ggt	gat	cga	gcc	cgt	gat	tca	gag	gac	2544
256	Tyr	Leu	Leu	Leu	Thr	Lys	His	Gly	Asp	Arg	Ala	Arg	Asp	Ser	Glu	Asp	
257			835					840					845				
259	agc	tgg	ggc	acc	tgg	gag	gca	cag	cct	gtc	aaa	gtc	gtg	cct	cag	gtg	2592
260	Ser	Trp	Gly	Thr	Trp	Glu	Ala	Gln	Pro	Val	Lys	Val	Val	Pro	Gln	Val	

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261	850	855	860	
263	gag act gtt gac acc ctg aga agc atg cag gtg gat aat ctt tta cta	2640		
264	Glu Thr Val Asp Thr Leu Arg Ser Met Gln Val Asp Asn Leu Leu Leu			
265	865	870	875	880
267	gtt gtc atg cag tct gcg cat ctc aca att cag aga aaa gct ttc cag	2688		
268	Val Val Met Gln Ser Ala His Leu Thr Ile Gln Arg Lys Ala Phe Gln			
269		885	890	895
271	cag tcc att gag gga ctt atg act ctg tgc cag gag cag aca tcc agt	2736		
272	Gln Ser Ile Glu Gly Leu Met Thr Leu Cys Gln Glu Gln Thr Ser Ser			
273		900	905	910
275	cag ccg gtc atc gcc aaa gct ttg cag cag ctg aag aat gat gca ttg	2784		
276	Gln Pro Val Ile Ala Lys Ala Leu Gln Gln Leu Lys Asn Asp Ala Leu			
277		915	920	925
279	gag cta tgc aac agg ata agc aat gcc att gac cgc gtg gac cac atg	2832		
280	Glu Leu Cys Asn Arg Ile Ser Asn Ala Ile Asp Arg Val Asp His Met			
281		930	935	940
283	ttc aca tca gaa ttt gat gct gag gtt gat gaa tct gaa tct gtc acc	2880		
284	Phe Thr Ser Glu Phe Asp Ala Glu Val Asp Glu Ser Glu Ser Val Thr			
285	945	950	955	960
287	ttg caa cag tac tac cga gaa gca atg att cag ggg tac aat ttt gga	2928		
288	Leu Gln Gln Tyr Tyr Arg Glu Ala Met Ile Gln Gly Tyr Asn Phe Gly			
289		965	970	975
291	ttt gag tat cat aaa gaa gtt gtt cgt ttg atg tct ggg gag ttt aga	2976		
292	Phe Glu Tyr His Lys Glu Val Val Arg Leu Met Ser Gly Glu Phe Arg			
293		980	985	990
295	cag aag ata gga gac aaa tat ata agc ttt gcc cgg aag tgg atg aat	3024		
296	Gln Lys Ile Gly Asp Lys Tyr Ile Ser Phe Ala Arg Lys Trp Met Asn			
297		995	1000	1005
299	tat gtc ctg act aaa tgt gag agt ggt aga ggt aca aga ccc agg tgg	3072		
300	Tyr Val Leu Thr Lys Cys Glu Ser Gly Arg Gly Thr Arg Pro Arg Trp			
301		1010	1015	1020
303	gcg act caa gga ttt gat ttt cta caa gca att gaa cct gcc ttt att	3120		
304	Ala Thr Gln Gly Phe Asp Phe Leu Gln Ala Ile Glu Pro Ala Phe Ile			
305	1025	1030	1035	1040
307	tca gct tta cca gaa gat gac ttc ttg agt tta caa gcc ttg atg aat	3168		
308	Ser Ala Leu Pro Glu Asp Asp Phe Leu Ser Leu Gln Ala Leu Met Asn			
309		1045	1050	1055
311	gaa tgc att ggc cat gtc ata gga aaa cca cac agt cct gtt aca ggt	3216		
312	Glu Cys Ile Gly His Val Ile Gly Lys Pro His Ser Pro Val Thr Gly			
313		1060	1065	1070
315	ttg tac ctt gcc att cat cgg aac agc ccc cgt cct atg aag gta cct	3264		
316	Leu Tyr Leu Ala Ile His Arg Asn Ser Pro Arg Pro Met Lys Val Pro			
317		1075	1080	1085
319	cga tgc cat agt gac cct cct aac cca cac ctc att atc ccc act cca	3312		
320	Arg Cys His Ser Asp Pro Pro Asn Pro His Leu Ile Ile Pro Thr Pro			
321		1090	1095	1100
323	gag gga ttc agg ggt tcc agc gtt cct gaa aat gat cga ttg gct tcc	3360		
324	Glu Gly Phe Arg Gly Ser Ser Val Pro Glu Asn Asp Arg Leu Ala Ser			
325	1105	1110	1115	1120

## VERIFICATION SUMMARY

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L:12 M:270 C: Current Application Number differs, Replaced Current Application No  
L:12 M:271 C: Current Filing Date differs, Replaced Current Filing Date  
L:20 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:31 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:420 M:334 W: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:1  
L:445 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:456 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:467 M:258 W: Mandatory Feature missing, <220> FEATURE:  
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L:1279 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1290 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1301 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1312 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1323 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1334 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1345 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1356 M:258 W: Mandatory Feature missing, <220> FEATURE:

## VERIFICATION SUMMARY

PATENT APPLICATION: US/09/676,436

DATE: 11/07/2001

TIME: 15:14:34

Input Set : A:\RTS-0169\_Seq\_ASCII.txt

Output Set: N:\CRF3\11072001\I676436.raw

L:1367 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1378 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1389 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1400 M:258 W: Mandatory Feature missing, <220> FEATURE:  
L:1411 M:258 W: Mandatory Feature missing, <220> FEATURE: